UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/368,989	08/05/99	STEVENS	F 0003/00332

HM22/0830

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EXAMINER	
COOK, L	
ART UNIT	**PAPER NUMBER**
1641	5

DATE MAILED: 08/30/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/368,989	Stevens et al.
Examiner	**Group Art Unit**
Lisa V. Cook	1641

☒ Responsive to communication(s) filed on *Aug 5, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-20* is/are pending in the applicat

Of the above, claim(s) *1-9 and 15-20* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *10-14* is/are rejected.

☒ Claim(s) *10-14* is/are objected to.

☒ Claims *1-20* are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *1*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Please note that the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Group Art Unit **1641**. All communications should be directed to **Lisa V. Cook**, whose telephone number is **(703) 305-0808**.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9 are drawn to a molecule with two antigen binding sites, classified in class 530, subclass 305 for example.

II. Claims 10-14 are drawn to a molecule capable of binding a plurality of antigens, classified in class 530, subclass 402 for example.

III. Claims 15-20 are drawn a method of detecting a protein, classified in class 435, subclass 7.1 for example.

3. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are directed to different synthetic products having different requirements/limitations. The molecule of invention I will bind with two antigen binding sites while the molecule of invention II will bind a plurality of antigens. Thus the molecules have different modes of operation.

Inventions (I-II) and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process can be practiced with materially different products. Specifically, the method of invention IIII can utilize either the product of invention I or the product of invention II.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and **do not** represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes foreign patents and applications as well as literature searches.

5. During a telephone conversation with Micheal J. Cherskov (Reg. No. 33664) on 8/18/00 a provisional election was made without traverse to prosecute the invention of II, claims 10-14. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-9 and 15-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

7. Currently claims 10-14 are pending and currently under consideration.

Drawings

8. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect can be deferred until the application is allowed by the examiner.

Information Disclosure Statement

9. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 lists the references, they have not been considered.

Oath/Declaration

10. A new oath or declaration is required because the second inventor (Schiffer) did not provide date of signature. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

11. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

12. The disclosure is objected to because of the following informalities:The attempt to incorporate subject matter into this application by reference to web sites http:/www.rcsb.org/pdb/ and http:/www.sdsc.edu/ is improper because Applicants have embedded a hyperlink which is impermissible and requires deletion. (see page 10 of the disclosure). This attempt to incorporate subject matter into the patent by reference is improper because PTO policy does not permit the PTO to link to any commercial sites since the PTO exercises no control over those organizations, views or accuracy of the information contained on those outside sites. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 10, the use of the phrase "plurality of antigens" is vague and indefinite. It is not clear if the term is intended to designate infinite/numerous binding capability, while the claim appears to depict a dual binding molecule. It is suggested that applicant utilize consistent claim language to further clarify the claim (i.e. dual in the preamble of define how the cited molecule will have a number of different binding sites). Please explain.

B. Claim 10 is vague and indefinite in reciting "capable of". It is not clear if the molecule will bind and antigen or not? Please correct appropriately.

C. Claim 10, steps a) and b) are vague and indefinite because it is not known if the first antigen non-binding region and the second antigen non-binding regions are encompassed with in the recited moiety or are separate compounds. If applicant intends to claim a moiety made up of these compounds, it is suggested that the claim read " a first moiety with a first antigen binding region bound to a first antigen-non-binding region". Please clarify.

D. Claim 10 is vague and indefinite because it is not clear what applicant means in reciting "at opposite ends of the molecule". Is it Applicants intent to claim the "flip" technique found in the disclosure page 6, lines 1-3 or the β-sheet configuration found in dimer formation. Please explain.

E. Claim 12 is vague and indefinite in utilizing the term "genetic products". Because the term is not defined in the specification the metes and bounds of the claim can not be determined. Is it applicant intent to mean any product containing a gene, derived from a gene, or employed in genetic analysis? Please define.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 10-14 are directed to non-statutory subject matter. The inventions as claimed read on any molecule, where the molecule includes products of nature. Non-naturally occurring compositions are considered to be patentable subject matter within the scope of 35 U.S.C. 101. Compositions that are products of nature are considered non-statutory and non-patentable. See Official Gazette, 1077 O.G. 24, April 21, 1987. It is recommended that the claims incorporate the claim language, "isolated" or "purified" to overcome this rejection.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 10 – 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoogenboom et al. (WO 93/06213).

Hoogenboom et al. disclose methods of producing chimeric antibodies. In one embodiment a polypeptide comprising a heavy or light chain variable domain of a non-human antibody specific for an antigen of interest (applicant's first moiety) is combined with a complementary light or heavy chain variable domain (applicant's second moiety) to form a library of antibody polypeptide dimers with antigen binding sites. (See Abstract). In this reference structural reshaping of the beta-sheets or molecular remodeling was successfully accomplished. (Page 2, lines 17-37).

II. Claims 10 – 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevens et al. (Protein Science, 1995, Vol.4, pages 421-432).

Stevens et al. teach recombinant generation techniques involving immunoglobulin variable domains. The $_{k}$IV amino acid sequence data was used to construct synthetic genes encoding the VL portions of proteins LEN, REC, and SMA. (Page 423, 2nd column). The three closely homologous protein products of the light-

chain variable-region single-gene family V_kIV were studied. Immunochemical and biophysical comparisons demonstrated that the recombinant V_kIV products have tertiary structural features comparable to those of patient derived proteins. (Abstract) Light-chain dimer formation of these molecules was determined via crystallography. (Page 427, 2nd column, last paragraph). Specifically, rLEN-REC hybrid was constructed. These dimers exhibited unusually high dimerization constants that were explained by the unusual amino acid located within their β-sheet configurations. (Pages 427, 3rd paragraph). The gene constructs are taught to be useful in as antibody reagents for medical and diagnostic analyses. (Page 421, 2nd column). Specifically, rLEN-REC hybrid was constructed.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102((e), f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stevens et al. (Protein Science, 1995, Vol.4, pages 421-432) or Hoogenboom et al. (WO 93/06213) in view of Goling (Journal of Immunology, 1980, 124(5), pages 2082-2088)-Abstract Only and Skoog et al. (Scand. J. Immunolgy, 1980, 11(4), pages 369-376)-Abstract Only.

Please see Hoogenboom et al. (WO 93/06213) and Stevens et al. as set forth above.

Hoogenboom et al. (WO 93/06213) and Stevens et al. differ from the instant invention in not specifically reciting the weight requirements of claim 14. (between 20,000 and 30,000 daltons).

However, both references of Goling and Skoog et al. teach that the protein structure in the range of 20,000 to 30,000 daltons is important in surface receptor, immunogobulin activity.

Hoogenboom et al., Stevens et al., Goling, and Skoog et al. are analogous art, because all four references teach methods concerning proteins.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize a molecule weighing between 20,000 and 30,000 daltons as taught by Goling and Skoog et al. in the method/product of Hoogenboom et al. or Stevens et al. to produce a dimeric antigen binding molecule.

A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such compounds, because such weight ranges were previous demonstrated. One of ordinary skill in the art would have been motivated to do this because Goding taught that protease cleavage of the lymphocyte surface IgD typically resulted in one light chain disulfide bond fragment weighting 30,000 daltons. Skooog et al. further taught that SDS polyacrylamide gel electrophoresis exhibited a broad peak at the molecular weight range of 20,000-35,000 daltons for surface receptors.

17. For reasons aforementioned, no claims are allowed.

Remarks

18. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Raffen et al. presentation on in vitro characterization of light chain amyloidsis using recombinant light chain variable domains. Argonne National Lab., Argonne, Il 60439 USA. Biophysical Journal, 1996, Vol.70, No.2, pp. A65. 40th Annual Meeting of the Biophysical Society Baltimore, Maryland, USA. February 17-21,1996.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday – Friday from 8:00AM – 4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
Art Unit 1641
CM1-7D16
(703) 305-0808
August 25, 2000

LONG V. LE
SUPERVISORY PATENT EXAMINER
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